DATA EVALUATION RECORD

Pine Oil Blend CSMA 1687
MRID: 40253503

Acute Dermal Toxicity (LD50) Study (Rabbit)
OPPTS 870.1200

Prepared for

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EPA WAM: Killian Swift

This review may have been altered by EPA subsequent to the contractor's signatures above.

EPA Reviewer: Tim McMahon, Ph.D. **Signature:**
Senior Toxicologist, Antimicrobials Division (7510C) **Date** 1-05-07

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STUDY TYPE: Acute Dermal Toxicity - rabbit; OPPTS 870.1200 [§81-2]; OECD 402.

PC CODE: 067002 **DP BARCODE:** N/A
SUBMISSION NO.: N/A

TEST MATERIAL (PURITY): Pine Oil Blend CSMA 1687 (97.9% active ingredients)

SYNONYMS:

CITATION: Naas, D.J. (1987) Acute Dermal Toxicity (LD50) Study in Albino Rabbits with Pine Oil Blend CSMA 1687. WIL Research Laboratories, Inc., Ashland, Ohio. WIL Study No.: WIL-114002. June 19, 1987. MRID 40253503. Unpublished.

SPONSOR: Chemical Specialties Manufacturers Association, Suite 1120, 101 Connecticut Avenue, NW, Washington, DC 20036

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 40253503), young adult New Zealand White rabbits (5/sex) were dermally exposed to Pine Oil Blend CSMA 1687 (97.9% a.i.; batch/lot # not provided). The test article was applied to 20-25% of the body surface area for 24 hours at a dose of 2000 mg/kg bw. Animals were observed for 14 days.

None of the rabbits died prior to scheduled sacrifice and no significant systemic treatment-related findings were observed. No treatment-related clinical signs, necropsy findings, or changes in body weight were observed. Treatment-related findings were as follows: moderate to severe erythema, moderate edema, fissuring, desquamation, blanching, scabbing, and exfoliation. Skin irritation reactions were observed immediately after administration, but the severity and incidence rates decreased over the observation period with only minor irritations noted at study termination. Therefore, the LD_{50} value of Pine Oil Blend CSMA 1687 for both sexes is greater than 2000 mg/kg bw when applied to the shaved, intact skin of rabbits.

Pine Oil Blend CSMA 1687 is of **Low Toxicity** based on the results of this test. The dermal LD_{50} for rabbits of both sexes was determined to be greater than 2000 mg/kg bw

This acute dermal toxicity study is classified as **ACCEPTABLE-GUIDELINE**. This study satisfies the guideline requirement for an acute dermal toxicity study (OPPTS 870.1200; OECD 402) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. The study was conducted in accordance with GLP regulations with the following exception: The rabbits were shaved three times throughout the 14-day study period rather than twice a week as required by the study protocol. The study director did not believe that this deviation interfered with the scientific quality, integrity, or objective of the study.

I. MATERIALS AND METHODS

A. MATERIALS:

1. TestMaterial: Pine Oil Blend CSMA 1687

Description:	Clear pale yellow liquid; stable at ambient conditions but sparks and flames must be avoided (MSDS pp. 29-30)
Lot/Batch #:	Not provided
Purity:	Alpha terpineol 64.6%, Dipentene 16.8%, and Terpene alcohols 16.5% (MSDS pp. 29-30)
CAS # of TGAI:	

2. Vehicle and/or positive control: The test article was used as supplied.

3. Test animals:

Species:	Rabbit	
Strain:	New Zealand White	
Age/weight at dosing:	Young adult; 1990 to 2380 grams	
Source:	Mohican Valley Rabbitry, Loudonville, Ohio	
Housing:	Individually housed in suspended wire-mesh cages	
Diet:	Purina® Cerified Rabbit Chow® #5322 was available *ad libitum.* Contaminant analysis was performed by the manufacturer and no microbiological or chemical contaminants were found.	
Water:	Tap water was available *ad libitum.* The water was analyzed twice yearly and no chemicals or microbiological contaminants were found.	
Environmental conditions:	**Temperature:**	20-22°C
	Humidity:	40-62%
	Air changes:	10/hr
	Photoperiod:	12 hrs dark/12 hrs light
Acclimation period:	7 days	

B. STUDY DESIGN and METHODS:

1. In life dates - Start: February 2, 1987 End: February 16, 1987

2. Animal assignment and treatment - Animals were assigned to the test groups noted in Table 1. Animals received a single 2000-mg/kg dose of Pine Oil Blend CSMA 1687 applied dermally using a glass rod to shaved dorsal skin. Approximately 20-25% of the total body surface was covered. After dosing, gauze binders were placed over the application sites and secured with nonirritating tape. Collars were placed on the rabbits for the duration of the 24-hour exposure period. After 24 hours, the gauze binders and collar were removed;residual test article was removed with a wet paper towel. The rabbits were observed for mortality and clinical signs at 1, 2.5, and 4 hours after dosing and once daily thereafter for 14 days. Body weights were measured on days 0, 7, and 14. Survivors were sacrificed and a necropsy was performed.

TABLE 1. Doses, mortality/animals treated

Dose (mg/kg bw)*	Males	Females	Combined
2000	0/5	0/5	0/10

* In accordance with the study protocol, a single dosage level of 2000 mg/kg bw was administered because the LD_{50} was expected to be greater than 2.0 g/kg. If no compound-related mortality occurs at 2.0 g/kg, then no further testing is required.

3. Statistics - The exact dermal LD_{50} could not be calculated since no mortality was observed at the limit dose of 2.0 g/kg.

II. RESULTS AND DISCUSSION:

A. MORTALITY - None of the rabbits died prior to scheduled sacrifice.

B. CLINICAL OBSERVATIONS - The test article caused moderate to severe erythema, moderate edema, and fissuring (1/5 females) after 24 hours. Fissures were observed in all rabbits by Day 3 with 2/5 males displaying blanching. Desquamation was noted in 1/5 males and 2/5 females on Day 4. Dermal irritation responses subsided throughout the study period; however, fissures were observed in 2/5 males and 3/5 females, desquamation was reported in 5/5 males and 3/5 females, and exfoliation was seen in 1/5 females at study termination. No other treatment-related clinical signs were noted. Occasional observations of dried red material around the mouth, wet brown urogenital staining, and diarrhea were noted. One female had the plastic restraint collar caught in the mouth on day 0.

C. BODY WEIGHT - No significant changes in body weights were observed throughout the study period.

D. NECROPSY - At necropsy, 5/10 rabbits had encrusted and/or thickened application sites, but there were no significant changes concerning the tissues examined internally.

E. REVIEWER'S CONCLUSIONS: Pine Oil Blend CSMA 1687 is of low toxicity based on the absence of mortality and other major treatment-related effects at 2000 mg/kg bw.

F. DEFICIENCIES - The following deficiencies were noted:

- The lot/batch # of the test article was not provided; however, a MSDS was provided. Complete characterization of the test article used was not included in the study report.
- The method of animal randomization was not provided.
- The rabbits were shaved three times throughout the 14 day study period rather than twice a week as required by the study protocol.

These deficiencies are considered to be minor and would not interfere with the interpretation of the study.

G. STUDY CLASSIFICATION: This acute dermal toxicity study in the rabbit is classified as **ACCEPTABLE-GUIDELINE.** This study satisfies the guideline requirement for an acute dermal toxicity study (OPPTS 870.1200; OECD 405) in the rabbit.

III. REFERENCE

Draize, J.H. (1965) The Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics, Der. Tox., pp. 46-59. Assoc. of Food and Drug Officials of the U.S., Topeka, Kansas.